REMARKS

A. Regarding the Amendments

As amended, the claims are supported by the specification and the original claims and do not add new matter. The amendments do not require a new search or raise new issues for consideration because they merely address issues already raised by the Examiner or define Applicant's invention more clearly. It is submitted that the amendments place the claims in condition for allowance or in better condition for appeal by reducing the number of issues for consideration on appeal. The amendments were not made earlier in the prosecution because it is maintained that the previously pending claims were allowable. Applicant submits that the amendments to the claims are for clarity and should not be construed as amendments affecting patentability under Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 234 F.3d 558, 56 USPQ2d 1865 (Fed. Cir. 2000) (en banc). Since the amendments do not add new matter or require a new search or consideration, and place the claims in condition for allowance or in better condition for appeal, entry of the amendment is respectfully requested. After entry of the amendments, claims 1-47 and 63-68 will be pending. Claims 18 and 63 have been amended as set forth in the attached "Version With Markings To Show Changes Made."

B. Objections to the Specification

The specification is objected to in Paper No. 9 because the ATCC accession number is omitted on page 14. Applicant respectfully draws the Examiner's attention to the amended language of the specification. As amended, there is no reference to an ATCC deposit or number. Accordingly, removal of the objection is respectfully requested.

C. Rejections Under 35 U.S.C. §112, first paragraph

Claims 1 to 47 and 63 to 68 are rejected as allegedly not enabling under 35 U.S.C. §112, first paragraph. The rejection is respectfully traversed.

Initially, the Examiner has alleged that "while the claims no longer encompass a method in which the cells in and of a subject's body are contacted with the agent, the claims still read on a method comprising contacting whole, live cells in isolation of the subject's body with an agent." It is respectfully submitted that the situation described by the Examiner, "contacting whole, live cells in isolation of the subject's body with an agent" is an *ex vivo* method of treatment. *Ex vivo* is a type of *in vitro* culture method. The claims specifically recite an *in vitro* method. In Paper No. 7 the claims were rejected as non enabled because the substrate used, coelenterazine, was alleged to be toxic to humans. Applicant respectfully drew the Examiner's attention to the fact that the claimed invention is a screening method, not a therapeutic method. Again, Applicant brings this point to the Examiner's attention. The limitation "[a]n *in vitro* method" is contained in all of the independent claims of the invention. It is respectfully submitted that the claimed method of the invention is not used in humans. The method of the claimed invention does not entail administration of coelenterazine to humans. However, the claimed invention does disclose administration of coelenterazine to cells *in vitro*, including *ex vivo* methods. It is respectfully submitted that the claims of the invention are enabling, as one of skill in the art would have known, at the time of filing of the invention, how to use the methods of the claimed invention.

Additionally in Paper No. 9, it is alleged that claim 63 has not been amended to recite the limitation of the method being an *in vitro* method. Applicant respectfully draws the Examiner's attention to amended claim 63, which includes the limitation "*in vitro*." As such, claim 63 will be addressed throughout this response as containing the same limitation as claims 1, 18 and 31.

The Examiner has alleged that the specification teaches that coelenterazine can be added during culturing of the cells containing a *Renilla* luciferase. Applicant respectfully disagrees. The Examiner has pointed to the paragraph on pages 19-20, citing the portion of the specification that states, "[t]he cells containing a *Renilla* luciferase are cultured under conditions that allow expression of *Renilla* luciferase. The luciferase activity can then be measured *in vivo* or *in*

vitro... by providing the cell culture with the substrate coelenterazine." (Underlining added in Paper No. 9.) Applicant respectfully submits that this quote further supports Applicant's position that the coelenterazine is not included during culturing of the cells. The language in the specification, as cited above is noted to contain two sentences. In the first sentence the cells are cultured. In the second sentence it is stated, "activity can then be measured...by providing the cell culture with the substrate coelenterazine." In addition, the Examiner's attention is again respectfully drawn to the Examples section of the application, to the Example entitled "Assay for Luciferase Activity" on pages 25-26. This Example illustrates that coelenterazine is not included during cell culture. The cells are first cultured, then the coelenterazine is added to the cells and light emission is collected for fifteen seconds "immediately upon the addition of the substrate." Accordingly, Applicant maintains that the coelenterazine is not added during culture of the cells.

The Examiner also alleges that the specification does not exemplify methods using intact cells, nor does it give guidance in the specification, except for the paragraph on pages 19 and 20, that would teach one to practice the claimed method using intact and viable cells. Applicant respectfully submits that the disclosure on pages 19 and 20 is sufficient to guide one of skill in the art to practice the invention. On page 20, line 3, "whole cell" is given as an example. One of skill in the art could practice the methods of the invention using this disclosure. No further exemplification is required.

It is also alleged in Paper No. 9 that "coelenterazine is toxic to cells and that the toxicity of coelenterazine is amplified in the presence of certain other agents." The Examiner alleges that the specification provides insufficient guidance with regard to this issue. It is respectfully submitted that the specification does provide sufficient guidance with regard to the use of coelenterazine. In the claimed invention, coelenterazine is used in measuring the luciferase activity of the cell. The toxicity is not relevant, as coelenterazine is not used during culturing of cells, as set forth above. Additionally, with the *in vitro* limitation added to the claims, coelenterazine is not used in the body. Therefore, even if coelenterazine is toxic to the cells,

whether amplified by the presence of an agent or not, it is used only *in vitro* to determine the effect of the agent on cell proliferation. Administration of coelenterazine to living cells in the body is not claimed in the present application.

It is alleged in Paper No. 9 that "the specification does not teach how the effects of coelenterazine can be distinguished from the effects of the agent suspected of modulating cell proliferation." Applicant asserts, as set forth above, that coelenterazine is not included during culturing of cells. Therefore, any effect on proliferation is due solely to the agent. Coelenterazine, however, is added after culturing and light emission data is immediately collected. In the Examples section of the application, on pages 25-26, there is an Example entitled "Assay for Luciferase Activity." In the example, Applicant shows that coelenterazine is not included during cell culture. The coelenterazine is added to the cells and light emission is collected for fifteen seconds "immediately upon the addition of the substrate." As previously set forth by Applicant in Paper No. 8, cells will clearly not grow appreciably in only fifteen seconds. Therefore, there is not time for coelenterazine to have any observable effect on proliferation, whether alone or amplified by the presence of an agent. Additionally, it is noted that wells containing medium only were used as controls. (Specification, page 26.) The Examiner asserts that Applicant's position is in contradiction to the teachings of Dubuisson et al., however Applicant is not stating that coelenterazine cannot have an effect on proliferation, merely that in the method of the claimed invention, that there is not time for coelenterazine to have an effect on proliferation. Applicant is not contradicting the teachings of Dubuisson et al., but asserting the inapplicability of those teachings to the methods of the claimed invention.

Additionally, Paper No. 9 acknowledges that the addition of the *in vitro* limitation to claims 1, 18 and 31 resolves the issue of "how valid light emission data can be collected when the specification does not teach a method for distinguishing the toxic effect of coelenterazine from the effects of the agent that is being screened in practicing the claimed method" with regard to administering coelenterazine to a subject. However, the Examiner asserts that the rejection

stands with regard to whole, live cells in isolation of the subject's body. As set forth above, Applicant respectfully submits that the toxic effects of coelenterazine on proliferation are distinguishable from the effect on proliferation by the agent being screened. Therefore, as amended, claims 1, 18 and 31 claim a method from which valid light emission data can be collected. It is noted that claim 63 has also been amended to include the *in vitro* limitation. Accordingly, the same arguments pertain to claim 63.

It is also alleged in Paper No. 9 that exemplification of the claimed method is allegedly not commensurate in scope with the claims. Applicant respectfully disagrees. It is again alleged by the Examiner that the art is highly unpredictable, as evidenced by the Cree reference. However, it is Applicant's position that it is expected that the present invention would not have been predictable at the time of publication of the Cree reference. It is expected that the present invention would not have been obvious or predictable as of 1998. The Cree reference, as cited in Paper Nos. 7 and 9, states: "It is unlikely that molecular methods will fare much better." (Emphasis added.) However, it does not preclude the use of the present molecular methods. The Examiner alleges that a "strict correlation has not been established between *in vivo* bioluminescence and cell viability." It is respectfully submitted that the present invention is directed to *in vitro* methods, not *in vivo*. Additionally, the present invention does teach that a correlation exists between luminescence and determination of cell proliferation in that a measurement of luminescence will allow a determination in change of cell number. (Specification, page 20, line 26 to page 21, line 9.) This provides the correlation "between bioluminescence and cell viability and sensitivity to therapeutic agents." The correlation is used to determine the effect of an agent on cell proliferation, determine the cell proliferation of a cell or population of cells, or to screen mammalian cells to determine their susceptibility to treatment with an agent. Therefore, one of skill in the art practicing the present invention would not have to engage in undue experimentation.

Previously discussed in Applicant's response filed September 7, 2001, but not addressed by the Examiner's response in Paper No. 9 is the Examiner's previous assertion in Paper No. 7 that the specification allegedly does not exemplify the claimed method for screening mammalian cells to determine their susceptibility to treatment with an agent. It was also stated that there are allegedly no working examples that teach the claimed method and that the examples do not set forth a method for determining prokaryotic cell proliferation. Applicant respectfully traverses the rejection.

Throughout the specification and in the Examples section, Applicant discloses that treatment with an agent is related to cell proliferation. It is respectfully submitted that it is has been shown in the art that various mammalian cells may be screened in order to determine their susceptibility to treatment with a cancer agent. Exhibit B of Paper No. 8 sets forth the abstracts of four illustrative references that show this relationship. The Haug abstract, describes the finding that hydroxyurea, cytochalasin B, vinblastine, Razoxane and interferon all inhibit growth of murine fibrosarcoma cells. (Cell. Prolif. 1993 May; 26(3):251-61, attached to Paper No. 8 as Exhibit B.) Similarly, in the Malmberg abstract, the slow-down or arrest of growth of human ileocaecal adenocarcinoma cells, after exposure to 5-fluoro-2'-deoxyuridine is described. (Cell. Prolif. 1993 May; 26(3):291-303, attached to Paper No. 8 as Exhibit B.) The Shin reference shows the effects of a combination of 13-cRA, IFN-alpha and alpha-tocopherol on prevention of tumor recurrence. (J. Clin. Oncol. 2001 Jun 15; 19(12):3010-7, attached to Paper No. 8 as Exhibit B.) Finally, the Komatsu reference describes the inhibition of four out of five human tumor cell lines implanted into nude mice, by the agent cyclic hydroxamic-acid-containing peptide 31 (CHAP31). (Cancer Res. 2001 Jun 1; 61(11):4459-66, attached to Paper No. 8 as Exhibit B.) Similarly, the present invention exemplifies the effect of an agent on cellular proliferation and it is respectfully submitted that the relationship between cellular proliferation and susceptibility to treatment with an agent is well known in the art. Accordingly, Applicant respectfully requests that the present rejection be withdrawn.

Additionally, the Examiner notes on page 9 of Paper No. 9 that "other issues were raised in the previous Office Action, which were not addressed in Applicants [sic] remarks." Applicant is unclear as to what the Examiner is referring. It is assumed that because this comment is under the 35 U.S.C. §112, first paragraph section, that the issues allegedly not responded to are issues are in paragraph 5 of Paper No. 7. It appears that all issues in paragraph 5 of Paper No. 7 were responded to in Applicant's response mailed September 7, 2001. Clarification of this rejection is respectfully requested.

Accordingly, Applicant respectfully traverses the rejection of claims 1-47 and 63-68 as allegedly non enabled under 35 U.S.C. §112, first paragraph. As such, one of skill in the art would be able to practice the present invention, as set forth above, Therefore, claims 1-47 and 63-68 meet the enablement requirement of 35 U.S.C. §112, first paragraph. Accordingly, the removal of the rejection is requested.

D. <u>Rejections Under 35 U.S.C. §112, second paragraph</u>

Claims 1 to 47 and 63 to 68 are rejected as allegedly incomplete under 35 U.S.C. §112, second paragraph, for omitting essential steps. The rejection is respectfully traversed.

Applicant respectfully submits that the claims do not omit essential steps. As set forth by the Examiner in Paper No. 7, the steps allegedly omitted are: 1) a cellular lysate is prepared; 2) coelenterazine is added to the lysate; and 3) light emission data is collected from cells in the presence and absence of an agent. Applicant respectfully submits that these steps are not required for the practice of the present invention.

Applicant has reviewed the Examiner's arguments and maintains that the above steps are not necessary steps. Initially, a step requiring that a cellular lysate is prepared is not necessary. Where lysing is used in the invention, it is a part of measuring the light emission data. However,

it is Applicant's position that lysing the cells is not necessary to measuring light emission data. It is Applicant's position that lysing of the cells is not necessary to measure the light emission data. As coelenterazine is hydrophobic, it may penetrate the cells without the assistance of a detergent to make the cell membrane permeable. Additional methods of screening cells are available to one of skill in the art besides lysing the cells. These other methods might include the use of the tetrazoleum component MTT or use of Trypan Blue. Both would allow assays of cellular proliferation without lysing the cells. Because other methods of screening cells are available and are known to those of skill in the art, Applicant respectfully submits that no steps have been omitted from claims 1-17, 18-30, 31-47 or 63-68. It is therefore requested that the rejection be removed.

Additionally, it is Applicant's position that a step requiring that coelenterazine be added to the lysate is not necessary. As set forth above, lysing of the cells is not necessary. Additionally, when the cells are lysed, the coelenterazine may be added as the cells are being lysed or after the cells are lysed. (Specification, p. 20.) Therefore it is not only unnecessary, but incorrect to add a step to the claims that requires coelenterazine must be added to the lysate.

Finally, it was alleged in Paper No. 7 that the claims were missing a step to "light emission data is collected from cells in the presence and absence of an agent." In Paper No. 9, the Examiner has stated that this allegedly omitted step has been resolved by the addition of language comparing the emissions from cells in the presence and absence of an agent. However, it is stated in Paper No. 9 that claim 63 does not contain any such language. Applicant respectfully disagrees. The Examiner's attention is respectfully drawn to claim 63, which claims "measuring light emissions from the cells in the presence and absence of the agent, wherein a difference in light emissions is indicative of the cells' susceptibility to treatment with the agent." Applicant submits that this claim language contains the requirement of comparing the emissions in the presence and absence of the agent, as a difference would not be detectable without such a

comparison. Accordingly, it is submitted that inclusion of the allegedly omitted steps would be unnecessarily limiting.

As the allegedly missing steps of the claimed invention are either nonessential or are included, as set forth above, it is respectfully requested that the rejection of claims 1-47 and 63-68 under 35 U.S.C. §112, second paragraph as allegedly omitting essential steps be withdrawn.

Claims 1-47 and 63-68 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention. Applicant respectfully traverses the rejection. Applicant respectfully submits that the argument presented in Paper No. 8 remains the Applicant's position.

The Examiner's rejection of these claims is in regard to the terms "an agent" in line 3 of claim 1, "a cell" in line 3 of claim 18, "an agent" in line 5 of claim 31 and "cells" in line 3 of claim 63. Applicant respectfully submits that the use of these terms in the preamble of each respective claim is not limiting. Applicant respectfully stands by the statements Applicant made in Paper No. 8. The rejection of claims 1-17 alleges that the phrase "an agent" in line 3 of claim 1 is indefinite. This allegation is based on the fact that the term "an agent" is used in line 1 of the claim and therefore it is allegedly indefinite whether use of the term in line 3 refers to the same agent as in line 1. The use of the term "an agent" in line 1 is part of the preamble of the claim. Generally, a preamble is not considered limiting to a claim unless it breathes life and meaning into the claim. (See MPEP 2111.02.) In the present invention, the claim following the transitional phrase "comprising" stands alone. It is therefore unnecessary for the term "an agent" in line 1 to serve as an antecedent basis for the use of "an agent" in line 3, or for the term "agent" in line 3 to be preceded by a definite article. As such, use of the indefinite article "an" is proper in line 3. This argument applies equally to the rejections of claims 18, 31 and 63.

In response to Applicant's response mailed September 7, 2001, the Examiner's has stated that the preambles of claims 1, 18, 31 and 63 do breathe life and meaning into those claims, as required under MPEP 2111.02. The Examiner then poses the question:

> "In view of [MPEP 2111.02]...the Examiner wonders if applicant would still argue that the body of each claim 'stands alone.' For example, would a claim to a method for determining the effect of an agent *be* a method for determining the effect of the agent, when the method does not comprise a step of 'determining the effect of the agent.'"

In response to the Examiner's question, Applicant maintains that with regard to the terms "an agent" in line 3 of claim 1, "a cell" in line 3 of claim 18, "an agent" in line 5 of claim 31 and "cells" in line 3 of claim 63, the claims do stand alone.

As cited by the Examiner, MPEP 2111.02 in part states that "[i]f the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction." With regard to the terms "an agent" in line 1 of claim 1, "a cell" in line 1 of claim 18, "an agent" in line 1 of claim 31 and "cells" in line 2 of claim 63, these terms are part of the intended use of the invention. The claimed invention is "An *in vitro* method for determining the effect of an agent on cell proliferation..." (claim 1, emphasis added). The word "for" is defined by Merriam-Webster's Collegiate Dictionary as "a function word to indicate purpose." (See www.webster.com.) Accordingly, the language of the prepositional phrase beginning with the word "for" in the preamble of claims 1, 18 and 31 indicates the purpose of the claim, and is therefore not considered a limitation and "and is of no significance to claim construction." (MPEP 2111.02.) As the phrase is of no significance in claim construction, the occurrence of the phrases "an agent" in line 3 of claim 1, "a cell" in line 3 of claim 18, "an agent" in line 5 of claim 31 are the first occurrences of those

terms and should therefore be preceded with an indefinite article. Similarly, the preposition "to" is defined by Merriam-Webster's Collegiate Dictionary as "a function word to indicate purpose, intention, tendency, result, or end." (See www.webster.com.) Accordingly, the language of the prepositional phrase beginning with the word "to" in the preamble of claim 63 indicates the purpose of the claim, and is therefore not considered a limitation and "and is of no significance to claim construction."

As the use of indefinite terms "an agent" in line 3 of claim 1, "a cell" in line 3 of claim 18, "an agent" in line 5 of claim 31 and "cells" in line 3 of claim 63 do not require an antecedent basis, as used, it is submitted that those claims are not indefinite under 35 U.S.C. §112. Accordingly, the removal of the rejection of claims 1-47 and 63-68 is respectfully requested.

Additionally, the Examiner has asserted that if the preamble is not limiting for the above terms, then it is not limiting for the insertion of the term "*in vitro*" added in Paper No. 8. Applicant respectfully disagrees. As set forth above, the phrase containing the above terms was part of a prepositional phrase indicating purpose of the claim. In contrast, the phrase "An *in vitro* method" is a structural limitation on the claim and, as set forth in MPEP 2111.02, is limiting upon the claim. The "*in vitro*" language does not appear elsewhere in the claim and is therefore limiting to the claim where it does appear. As such, it is respectfully submitted that the language of the claim, as presently pending is congruent, clear and definite. Accordingly withdrawal of the rejection of claims 1-47 and 63-68 as rejected under 35 U.S.C. §112, second paragraph, is respectfully requested.

Claims 18-30 are rejected under 35 U.S.C. §112, second paragraph, as indefinite for failure to point out and distinctly claim the subject matter which Applicant regards as the invention. Applicant respectfully traverses the rejection. Specifically, the Examiner has stated that the term "a corresponding change" in claim 18 is vague and indefinite. However, in the interest of placing these claims in position for acceptance, claim 18 has been amended. As

amended, the claim no longer contains the term "a corresponding change," as the word "corresponding" has been removed. Accordingly withdrawal of the rejection is requested.

E. Rejections Under 35 U.S.C. §103

Claims 1 to 47 and 63 to 68 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Cree in view of Virta, et al, Edinger, et al, Prosser, et al, and further in view of U.S. Pat. Nos. 5,292,658 A and 6,171,809 B1. The rejection is respectfully traversed.

35 U.S.C. § 103 requires that:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious to a person having ordinary skill in the art to which said subject matter pertains."

Additionally, for an invention to be obvious in light of a combination of references under 35 U.S.C. §103, 1) there must be a suggestion of motivation to combine the references, 2) there must be a reasonable expectation of success, and 3) the prior art references must teach or suggest all of the claim limitations. (See MPEP 2142). It is respectfully submitted that Cree in view of Virta, et al, Edinger, et al, Prosser, et al, and further in view of U.S. Pat. Nos. 5,292,658 A and 6,171,809 B1 does not meet these requirements, and therefore the claims are not obvious in light of these references.

Applicant's prior argument (in Paper No. 8) set forth how the combination of references lacked requirement 3 above, the references do not teach or suggest all of the claim limitations. Specifically, it was argued by Applicant in Paper No. 8 that none of the references cited as allegedly rendering the present invention obvious teach or suggest that the effect of an agent on cell proliferation may be tested via measurement of light emission using *Renilla* luciferase. There is no

suggestion or motivation to combine the references to achieve the claimed invention. The Examiner queries as to why the references were discussed individually when a 103 rejection is based on a combination of references. Specifically, the Cree reference was discussed first, as it was cited by the Examiner as the primary reference. Cree was shown to be lacking various features of the claimed invention. Then each of the secondary references was discussed individually to show how each reference did not teach the element lacking in the primary reference. The conclusion was therefore reached that in combination, the cited references did not teach all of the elements of the claimed invention. Therefore it was asserted that the rejection of claims 1-47 and 63-68 could not stand.

Specifically, Cree teaches determination of cell viability based on luminescence. It is ATP based. It lacks a teaching or suggestion of the use of luminescence using *Renilla* luciferase. None of the other references cited by the Examiner teach or suggest this missing element. Accordingly, the combination of references does not teach or suggest all of the claim elements of the claimed invention.

The remaining references are Virta, Edinger, Prosser and U.S. Pat. Nos. 5,292,658 A and 6,171,809 B1. These references are discussed individually below to show that none of the cited references, either alone or when combined with Cree or one another, teach or suggest the use of luminescence using *Renilla* luciferase. The Virta reference discusses the connection between prokaryotic cell viability and light emission, but uses a known agent to establish this connection. Virta contains no teaching or suggestion to use the process in reverse, using the light emission of *Renilla* luciferase to determine the effect of an agent of unknown properties on proliferation.

The Edinger reference also does not teach or suggest the use of *Renilla* luciferase to determine the effect of an agent on cellular proliferation. Accordingly, this reference does not teach or suggest the present invention.

The teachings of the Prosser reference and U.S. Pat. Nos. 5,292,658 A and 6,171,809 B1 cannot overcome the deficiencies of the Cree, Virta and Edinger references. None of the cited references in any combination teach or suggest the use of *Renilla* luciferase to determine the effect of an agent on cellular proliferation.

Cree, et al., Virta, et al, Edinger, et al, Prosser, et al, and U.S. Pat. Nos. 5,292,658 A and 6,171,809 B1 are provided as discussed above. None of the cited references, in any combination, teach or suggest all of the claimed aspects to the present invention. Accordingly, it is respectfully requested that this rejection of the claims under 35 U.S.C. § 103, be removed.

CONCLUSION

In Summary, for the reasons set forth herein, Applicant maintains that claims 1 to 47 and 63 to 68 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

No fee is deemed necessary in connection with the filing of this response. However, if any fee is deemed necessary, the Commissioner is authorized to charge (or apply any credits to) Deposit Account No.: 50-1355. The Examiner is invited to contact Applicant's undersigned representative if there are any questions related to this matter.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

The paragraph at page 4, lines 1-5, has been amended as follows:

The invention also provides a eukaryotic host cell containing an expression vector encoding *Renilla* luciferase. For example, the host cell can be any eukaryotic or mammalian cell such as a human cell. In one aspect, the cell is a HeLa cell. In a further embodiment, the HeLa cell has ATCC accession number [X.] CCL-2. In yet another aspect, the cell is a plant cell.

The paragraph at page 14, lines 7-12 has been amended as follows:

The invention provides a stably transfected mammalian cell containing a luciferase gene useful in measuring cell proliferation and the [affect] effect of an agent on cell proliferation. A HeLa cell was stably transfected with a *Renilla* luciferase gene as described in the examples below. This cell was expanded for cryopreservation. [A sample of this cell line has been deposited in the American Type Culture Collection, Rockville, Md., U.S.A. under the provisions of the Budapest Treaty [and assigned accession number ATCC XXXX.]

IN THE CLAIMS

18. (Twice Amended) An *in vitro* method for determining cell proliferation of a cell or population of cells comprising:

obtaining light emission data from a cell containing a *Renilla* luciferase polypeptide or a polynucleotide encoding a *Renilla* luciferase over a period of time wherein a change in light emission data is indicative of a [corresponding] change in cell proliferation.

63. (Twice Amended) [A] An *in vitro* method of screening mammalian cells to determine their susceptibility to treatment with an agent, comprising:

contacting cells containing a *Renilla* luciferase polypeptide or a polynucleotide encoding a *Renilla* luciferase with an agent; and

measuring light emissions from the cells in the presence and absence of the agent, wherein a difference in light emissions is indicative of the cells' susceptibility to treatment with the agent.